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(19) **United States**(12) **Patent Application Publication****PEREZ BAY et al.**(10) **Pub. No.: US 2021/0246224 A1**(43) **Pub. Date: Aug. 12, 2021**(54) **ANTIBODIES, AND BISPECIFIC
ANTIGEN-BINDING MOLECULES THAT
BIND HER2 AND/OR APLP2, CONJUGATES,
AND USES THEREOF**(52) **U.S. Cl.**
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35/00 (2018.01); **A61K 47/6879** (2017.08)(71) Applicant: **Regeneron Pharmaceuticals, Inc.,**
Tarrytown, NY (US)(57) **ABSTRACT**(72) Inventors: **Andres PEREZ BAY**, New York, NY
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The protein known as human epidermal growth factor 2 (HER2) is expressed in breast cancer cells and its expression is correlated with aggressive tumor growth. The present invention provides novel full-length human (IgG) antibodies that bind to human HER2 (monospecific antibodies) or to APLP2 (monospecific antibodies). The present invention also provides novel bispecific antibodies (bsAbs) that bind to both HER2 and APLP2 and mediate internalization and degradation of HER2 via the APLP2 complex in the presence of HER2-expressing tumors. Described are bispecific antigen-binding molecules and ADCs comprising a first antigen-binding domain that specifically binds human APLP2, and a second antigen-binding domain that specifically binds human HER2. The described bispecific ADCs are capable of inhibiting the growth of certain tumors expressing HER2 and may be useful for the treatment of breast cancer and disorders in which targeting a therapeutic agent to HER2-expressing tumor cell is desirable and/or therapeutically beneficial. For example, the bispecific antibodies of the invention are useful for the treatment of breast cancers, including breast cancers having a IHC2+ classification. The present invention also includes anti-HER2 antibody drug conjugates which inhibit tumor growth in vivo.

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